ABSTRACTS

Abstracts of Original Contributions: Young Investigators Awards Competition

The purpose of the Awards is to find and encourage the young investigators of promise on whom the future of cardiology depends. Any physician/scientist who is currently in a residency or fellowship training program or who has been in such a program within the past three years is eligible to submit an original investigation. Medical students and Ph.D. candidates are also eligible for the competition.

The Judging Committee has selected a finalist and a runner-up for each of the following categories: a) Clinical Investigations; b) Physiology, Pharmacology and Pathology; and c) Molecular and Cellular Cardiology.

The Awards will be presented at the 44th Annual Convocation Ceremony on Wednesday, March 22, at 6:00 p.m. The Young Investigator of the Year for each category will receive a plaque, a certificate and $2,000. The runners-up will each receive $500 and a certificate.

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Timothy J. Gardner, MD, FACC
Chairman
1995 Young Investigators Awards Committee

407 Young Investigators Awards Competition

Monday, March 20, 1995 10:30 a.m.–Noon
Ernest N. Moral Convention Center, Room 21

10:30

407-1 Cardio-Oesophageal Reflex: A Mechanism for "Linked Angina" in Patients with Angiographically Proven Coronary Artery Disease

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We have shown previously that oesophageal acid stimulation can reduce coronary blood flow in syndrome X patients suggesting the presence of a cardio-oesophageal reflex in humans. The presence of such a reflex in patients with coronary artery disease could explain the mechanism of "linked angina". To investigate this hypothesis we studied the effect of oesophageal acid stimulation on coronary blood flow in 14 patients with angiographically documented significant (>50% stenosis) coronary artery disease (CAD) and 18 heart transplant patients (HT). A fine tube was introduced through the patient's nose in to the distal oesophagus. A 3.6F intracoronary Doppler catheter was positioned in the proximal left anterior descending coronary artery. Coronary blood flow was calculated from measurements of coronary flow velocities and arterial cross-sectional area from quantitative angiography. Oesophageal instillation of 0.1 M hydrochloric acid and 0.9% saline was performed in random, double-blind fashion (60 ml over 5 minutes) and the measurements were repeated after each infusion. Nine patients in the CAD group reported their usual chest pain on acid instillation but none experienced any pain after saline infusion. None of the patients in the HT group experienced any chest pain on acid or saline infusion. There were no significant difference in systemic haemodynamics after the infusions in both groups. The coronary blood flow (CBF) was significantly reduced by acid oesophageal stimulation in the CAD group [CBF pre-acid 70.4 ± 14.3, CBF post-acid 46.4 ± 19.1 ml/min ($p < 0.01$)]. However, there was no significant difference in the CBF on saline infusion [73.5 ± 15.3 versus 72.5 ± 14 ml/min]. CBF in the HT group was unaffected by acid or saline infusion. In the 9 CAD patients who experienced angina on oesophageal acid infusion there was a significant reduction in CBF from 73.4 ± 12.9 to 34.6 ± 4.7 ml/min. However, in the 5 CAD patients who did not have any chest pain the CBF was unaffected by acid infusion [65.1 ± 16.7 versus 67.5 ± 16.7 ml/min]. *Conclusion:* Oesophageal acid stimulation can produce angina and significantly reduce coronary blood flow. The lack of any significant effect in the HT group, in whom the heart is denervated, suggests a neural reflex. The presence of such a reflex may be a mechanism for "Linked Angina" in patients with coronary artery disease.

10:45

407-2 Characterization of a Recombination Event Excluding the Harvey-ras-1 (H-ras-1) Locus in a Romano-Ward Long QT Syndrome Family Linked to Chromosome 11p15 and Isolation of a Polymorphic Repeat Telomeric to H-ras-1

M.W. Russell [1], L.C. Brody [2], D. Munroe [3], M. Dick II [1], F.S. Collins [2]. [1] *Univ. of Michigan, Ann Arbor, MI;* [2] *National Institutes of Health, Bethesda, MD;* [3] *Massachusetts Institute of Technology, Boston, MA*

The Romano-Ward Long QT Syndrome (RWLQTS) has been linked to chromosome 11p15.5 in several large families but demonstrates genetic heterogeniety. To date, there has been no published recombination between the Harvey-*ras*-1 (H-*ras*-1) locus and the RWLQTS in families linked to 11p15. The one LOD confidence interval for the RWLQTS gene is 3 cM from H-*ras*-1 (Keating et al, 1992). In a large multigenerational family, we demonstrate linkage of the RWLQTS to marker D11S932 on 11p15 with a LOD score of 3.14 at a theta of 0. The family was genotyped for the following 11p markers: H-*ras*-1 (2 markers), insulin growth factor II, tyrosine hydroxylase(TH), β-hemoglobin, D11S860, D11-S1363, D11S902, D11S1318, D11S1331, D11S1323, D11S1338, D11S909, D11S932, and D11S922. An unaffected individual and her two unaffected offspring carry the affected haplotype for the H-*ras*-1 region, spanning from H-*ras*-1 to TH. All three individuals had a QTc ≤ 0.40 seconds and no history of syncope making the diagnosis of RWLQTS extremely unlikely. This suggests that, although the gene for the RWLQTS is linked to chromosome 11p15 in this family, a recombination event may have occurred that separated the RWLQTS gene from the affected H-*ras*-1 region haplotype. Multipoint analysis indicates the most likely location for the RWLQTS gene in this family is near D11S932. To investigate a possible telomeric recombination event, cosmids telomeric to H-*ras*-1 were isolated. From one of these cosmids, a CA/CT repeat marker (78% heterozygosity) was characterized and its location telomeric to H-*ras*-1 was verified by interphase FISH. Genotyping of the family demonstrated that the same three unaffected individuals had the affected allele for this marker as well. However, due to the genotypes in the family, we could not exclude a telomeric recombination event. Based on its degree of heterozygosity, this marker will be extremely useful in the physical and genetic mapping of the 11p telomere. The recombination event in this family should aid the localization of the RWLQTS gene linked to chromosome 11p15. This is the first report of recombination between the H-*ras*-1 locus and the RWLQTS phenotype in a family in which RWLQTS is linked to 11p15.